II. Rejection Under 35 U.S.C. §102(b)

Claims 1-3, 10, 11, 21 and 23 are rejected under 35 U.S.C. §102(b) over EP '847. Applicants respectfully traverse this rejection.

Independent claim 1 is directed to a method for introducing a foreign matter into a cell, comprising the steps of: placing a small particle carrying a foreign matter at a part of a cell surface of a living cell, boring a hole in a cell wall and/or a cell membrane by irradiating and treating said part of the cell surface with a laser beam, and introducing the foreign matter into the living cell. Such a method is not disclosed in EP '847.

EP '847 discloses transducing a genetic substance into a microspore cell through a pore formed by a laser pulse thereby to express genetic information of the genetic substance. EP '847 at Abstract. In Example 1, cited in the Office Action, EP '847 teaches a DNA solution composed of (i) Okada solution, (ii) 15% mannitol, (iii) 10 μg/ml of pBI221, (iv) 10 μg/ml of pSBG102 (Hm^r), and (v) 50 μg/ml of Calf Thymus DNA. The solution is applied to a microspore cell and is laser processed. EP '847 at page 3, line 50 to page 4, line 15.

However, contrary to the position taken in the Office Action, EP '847 does not disclose the claimed "small particle carrying a foreign matter." EP '847 does not teach that the foreign matter is carried by a small particle. Instead, EP '847 merely discloses that the "foreign matter" (i.e., the plasmid pBI221) is in solution.

A. The Claim Language is Not Overly Broad

The Office Action takes the position that the language "a small particle carrying a foreign matter at a part of a cell surface of a living cell" is broad, and as such reads on the disclosure of EP '847. Applicants disagree.

Claim 1 specifically defines the limitation as "a small particle carrying a foreign matter." Claim 1 need not, and does not, specifically further define the small particle. However, this asserted breadth of the claim does not render the claim anticipated by EP '847. EP '847 must still disclose all of the claim limitations, regardless of the perceived claim scope. Because EP '847 does not disclose at least this limitation of claim 1, as described below, EP '847 does not anticipate the claimed invention.

B. EP '847 Does Not Disclose the Claimed Small Particle

The Office Action argues that EP '847's solution of water and DNA, with other materials, provides the claimed "small particle carrying a foreign matter." The Office Action argues that a negatively charged DNA forms on ionic bond with water, and thus the water is the claimed "small particle." Applicants disagree.

As is well known in the art, water is a solvent, which forms solutions with compatible materials. The Office Action argues that the solution formed by dissolving DNA in water forms ionically bound structures of water-DNA. This is incorrect.

A solution is defined as "a uniformly dispersed mixture at the molecular or ionic level, of one or more substances (the solute) in one or more other substances (the solvent)." See Hawley's Condensed Chemical Dictionary, 13th Ed., p. 1034 (1997) (copy attached). Accordingly, a solution does not include parts of the solute ionically bound to parts of the solvent, but merely a mixture of the respective components. Thus, in the example cited in the Office Action, the solution would include ionic DNA moieties and ionic water moieties, but would not include moieties that could be represented as DNA-water. The water in the example of EP '847 thus does not correspond to the claimed small particle.

In contrast to EP '847, the claimed invention provides a small particle carrying a foreign matter, which substance can be distinguished and isolated from a solution, if necessary. In fact, according to embodiments of the claimed invention, a solution is not even required, and the small particle carrying a foreign matter exists separate from a solution. Likewise, the small particle carrying a foreign matter can be introduced into a cell without the use of a solution.

C. Conclusion

For at least these reasons, claim 1 and claims 2-3, 10-11, 21 and 23 dependent therefrom are not anticipated by EP '847. Reconsideration and withdrawal of the rejection are respectfully requested.

III. Rejection Under 35 U.S.C. §103(a)

A. EP '847 and Gad

Claims 1-5, 10-11, 13-15, 20-21 and 23 are rejected under 35 U.S.C. §103(a) over EP '847 in view of Gad. Applicants respectfully traverse this rejection.

Claim 1 is described above. Independent claim 13 is directed to a method for introducing a foreign matter into a living cell, comprising the steps of: irradiating a living cell with a laser beam, removing a part of a cell wall of the living cell, exposing a part of the cell membrane, placing, on the exposed cell membrane, a liposome including a foreign matter, fusing the exposed cell membrane with the liposome, and thereby introducing the foreign matter into the living cell. Claims 1 and 13, and their dependent claims, would not have been obvious over the cited references.

As discussed above, EP '847 discloses transducing a genetic substance into a microspore cell through a pore formed by a laser pulse thereby to express genetic information of the genetic substance. EP '847 at Abstract. In Example 1, cited in the Office Action, EP '847 teaches a DNA solution composed of (i) Okada solution, (ii) 15% mannitol, (iii) 10 μg/ml of pBI221, (iv) 10 μg/ml of pSBG102 (Hm^r), and (v) 50 μg/ml of Calf Thymus DNA. The solution is applied to a microspore cell and is laser processed. EP '847 at page 3, line 50 to page 4, line 15. Gad is cited as disclosing the use of small liposome particles. The Office Action asserts that it would have been obvious to utilize the small liposome particles of Gad in the process of EP '847.

The requirements for a prima facie case of obviousness are specified and described in MPEP §2143. According to MPEP §2143, to establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation to modify the reference. Second, there must be a reasonable expectation of success. Third, the prior art reference must teach or suggest all the claim limitations. The references applied in the Office Action do not provide the necessary motivation for their combination, and fail to teach or suggest all the claim limitations.

1. The References Do Not Teach or Suggest a Small Particle Carrying a Foreign Matter

First, none of the references teach or suggest the limitation of the claimed invention that the small particle carries a foreign matter. Instead, as described in detail above, EP '847 teaches that the foreign matter is simply placed into solution, and not carried by a small particle. The water of EP '847 does not correspond to the claimed small particle, and does not carry the DNA as a foreign matter. Although Gad teaches the use of small liposome particles,

Gad does not teach that such particles can be employed as carriers of the foreign matter in methods including irradiating a living cell with a laser beam. Thus, the references fail to teach or suggest all of the claim limitations.

2. The References Are Improperly Combined

Second, the references are improperly combined in the Office Action, because neither reference provides any motivation for the asserted combination. For example, neither reference teaches or suggests why the small liposome particles of Gad could or should be incorporated into the plasmid solution of EP '847. EP '847 teaches that the plasmid solution provides the desired result of incorporating the plasmid into the cell. However, neither EP '847 nor Gad teach or suggest what effect would result if the plasmid were instead mixed with or attached to the small liposome particles of Gad. In the absence of any such teachings, one of ordinary skill in the art would not have been motivated to combine the references in the manner asserted in the Office Action.

Moreover, the reason, suggestion or motivation for combining the references "can not come from the applicant's invention itself." In re Oetiker, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). That is, the motivation for combining the references can not be a product of hindsight reconstruction of the claimed invention based on applicant's own disclosure. Such a hindsight reconstruction has clearly been made in the present Office Action. The Office Action asserts that the claimed invention would have been obvious based on a hindsight selection of the claimed limitations, as evidenced by the contradictory teachings of the cited references, none of which would suggest to one skilled in the art that the teachings could be combined and then further modified to render the claimed invention. Such a combination is improper because the

references, viewed by themselves and not in retrospect, must suggest the combination asserted by the Office Action. In re Shaffer, 229 F.2d 476, 108 USPQ 326 (C.C.P.A. 1956); In re Stoll, 523 F.2d 1392, 187 USPQ 481 (C.C.P.A. 1975). Here the references do not provide any motivation for combining the divergent teachings. The only motivation for combining the cited references in the manner asserted in the Office Action derives from the disclosure of the present application, which is clearly improper.

3. Conclusion

For at least these reasons, the claimed invention would not have been obvious to one of ordinary skill in the art over EP '847 in view of Gad. Reconsideration and withdrawal of the rejection are respectfully requested.

B. EP '847, Gad and Weber

Claims 1-5 and 9-15 are rejected under 35 U.S.C. §103(a) over EP '847 in view of Gad and further in view of Weber. Applicants respectfully traverse this rejection.

Claims 1 and 13 are discussed above. EP '847 and Gad are also discussed above.

Weber is cited in the Office Action as disclosing different laser irradiating devices, and the use of a microinjector. However, regardless of the teachings of Weber, neither EP '847 nor Gad teach or suggest all of the limitations of the claimed invention, as described above. Weber fails to overcome the deficiencies of EP '847 and Gad, and fails to provide the necessary motivation for combining EP '847 and Gad in the manner asserted in the Office Action.

Accordingly, any combination of EP '847, Gad and Weber fails to have rendered obvious the claimed invention. Reconsideration and withdrawal of the rejection are respectfully requested.

IV. Conclusion

In view of the foregoing, it is respectfully submitted that this application is in condition for allowance. Favorable reconsideration and prompt allowance of the claims are earnestly solicited.

Should the Examiner believe that anything further would be desirable in order to place this application in even better condition for allowance, the Examiner is invited to contact the undersigned at the telephone number set forth below.

Respectfully submitted,

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JAO:JSA

Attachment:
Hawley's Condensed Chemical Dictionary, 13th Ed., p. 1034 (1997).

Date: March 29, 2005

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Revised by

Richard J. Lewis, Sr.

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salt-gradient pond at Argonne National Laboratory 100 × 100 × 12 ft containing 2800 tons of water and 700 tons of sodium chloride has attained a bottom temperature approaching 180F.

solder. A low-melting alloy usually of the lead-tin type used for joining metals at temperatures below 425C. The solder acts as an adhesive and does not form an intermetallic solution with the metals being joined.
See brazing; welding.

solid. Matter in its most highly concentrated form, i.e., the atoms or molecules are much more closely packed than in gases or liquids and thus more resistant to deformation. The normal condition of the solid state is crystalline structure—the orderly arrangement of the constituent atoms of a substance in a framework called a lattice (see crystal). Crystals are of many types and normally have defects and impurities that profoundly affect their applications, as in semiconductors. The geometric structure of solids is determined by X rays that are reflected at characteristic angles from the crystalline lattices, which act as diffraction gratings.
See crystallography.

Some materials that are physically rigid, such as glass, are regarded as highly viscous liquids because they lack crystalline structure. All solids can be melted (i.e., the attractive forces acting between the crystals are disrupted) by heat and are thus converted to liquids. For ice, this occurs at 0C; for some metals the melting point may be as high as 3300C. Some solids convert by sublimation directly to a gas.

solid-state chemistry. Study of the exact arrangement of atoms in solids, especially crystals, with particular emphasis on imperfections and irregularities in the electronic and atomic patterns in a crystal and the effects of these on electrical and chemical properties.
See crystal; semiconductor; impurity.

"Solphenyl" *[Ciba-Geigy].* TM for fast-to-light direct dyes for cellulosic fibers.

solubility. The ability or tendency of one substance to blend uniformly with another, e.g., solid in liquid, liquid in liquid, gas in liquid, gas in gas. Solids vary from 0–100% in their degree of solubility in liquids, depending on the chemical nature of the substances; to the extent that they are soluble they lose their crystalline form and become molecularly or ionically dispersed in the solvent to form a true solution. Examples are sugar-water, salt-water. Liquids and gases are often said to be miscible in other liquids and gases, rather than soluble. Thus nitrogen, oxygen, and carbon dioxide are freely miscible in each other, and air is a solution (uniform mixture) of these gases.

The physical chemistry of solutions is an extremely complex mathematical subject in which the principles of electrolytic dissociation, diffusion, and thermodynamics play controlling parts. Raoult's law and Henry's law are also involved.
See miscibility; solution, true.

soluble oil. An oil (also called emulsifying oil) that, when mixed with water, produces milky emulsions. In some soluble oils the emulsion is so fine that instead of milky solutions in water, amber-colored, transparent solutions are formed. Typical examples are sodium and potassium petroleum sulfonates.
Use: Metal-cutting lubricants, textile lubricants, metal-boring lubricants, emulsifying agents.

soluble starch. See starch, modified.

"Solulan" *[Amerchol].* TM for an emulsifier and stabilizer emollient, solubilizer, or foam fortifier.
Use: In cold, cleansing or shave creams, lotions, mousses, soaps, and shampoos.

solute. One or more substances dissolved in another substance, called the solvent; the solute is uniformly dispersed in the solvent in the form of either molecules (sugar) or ions (salt), the resulting mixture is a solution.
See solution, true; solvent.

solution, colloidal. A liquid colloidal dispersion is often called a solution. Since colloidal particles are larger than molecules it is strictly incorrect to call such dispersions solutions; however, this term is widely used in the literature.

Note: Wolfgang Ostwald stated, "There are no sharp differences between mechanical suspensions, colloidal solutions, and molecular [true] solutions. There is a gradual and continuous transition from the first through the second to the third."
See colloid chemistry.

solution, true. A uniformly dispersed mixture at the molecular or ionic level, of one or more substances (the solute) in one or more other substances (the solvent). These two parts of a solution are called phases.
Common types are:
liquid-liquid: alcohol-water
solid-liquid: salt-water
solid-solid: carbon-iron

Solutions that exhibit no change of internal energy on mixing and complete uniformity of cohesive forces are called *ideal*; their behavior is described by Raoult's law. Solutions are involved in most chemical reactions, refining and purification, industrial processing, and biological phenomena.

The proportion of substances in a solution de-

pends on their limits of solution. The solubility of one substance in another is the maximum amount that can be dissolved at a given temperature and pressure. A solution containing such a maximum amount is *saturated*. A state of supersaturation can be created, but such solutions are unstable and may precipitate spontaneously.

solutrope. A ternary mixture having two liquid phases between which one component is distributed in an apparent ratio varying with concentration from less than 1 to greater than 1. In other words, the solute may be selectively dissolved in one or the other of the phases or solvents, depending on the concentration. This phenomenon has been compared to azeotropic behavior.

solvation. In the parlance of colloid chemistry, the adsorption of a microlayer or film of water or other solvent on individual dispersed particles of a solution or dispersion. The term *solvated hulls* has been used to describe such particles. It is also applied to the action of plasticizers on resin dispersions in plastisols.
See hydration (2).

Solvay process. (ammonia soda process). Manufacture of sodium carbonate (soda ash, Na_2CO_3) from salt, ammonia, carbon dioxide, and limestone by an ingenious sequence of reactions involving recovery and reuse of practically all the ammonia and part of the carbon dioxide. Limestone is heated to produce lime and carbon dioxide. The latter is dissolved in water containing the ammonia and salt, with resultant precipitation of sodium bicarbonate. This is separated by filtration, dried, and heated to form normal sodium carbonate. The liquor from the bicarbonate filtration is heated and treated with lime to regenerate the ammonia. Calcium chloride is a major by-product.
Note: Because this process requires much energy and pollutes streams and rivers with chloride effluent, many plants using it have closed, production being obtained from the natural deposits in the western U.S.

"Solvenol" ***[Aqualon].*** TM for a group of monocyclic terpene hydrocarbons with minor amounts of terpene alcohols and ketones.
Use: General solvent, rubber reclaiming.

solvent. A substance capable of dissolving another substance (solute) to form a uniformly dispersed mixture (solution) at the molecular or ionic size level. Solvents are either polar (high dielectric constant) or nonpolar (low dielectric constant). Water, the most common of all solvents, is strongly polar (dielectric constant 81), but hydrocarbon solvents are nonpolar. Aromatic hydrocarbons have higher solvent power than aliphatics (alcohols). Other organic solvent groups are esters, ethers, ketones, amines, and nitrated and chlorinated hydrocarbons.
The chief uses of organic solvents are in the coatings field (paints, varnishes, and lacquers), industrial cleaners, printing inks, extractive processes, and pharmaceuticals. Since many solvents are flammable and toxic to varying degrees, they contribute to air pollution and fire hazards. For this reason their use in coatings and cleaners has declined in recent years.
See individual compounds.

solvent, aprotic. A solvent that cannot act as a proton acceptor or donor, i.e., as an acid or base.

solvent drying. Removal of water from metal surfaces by means of a solvent that displaces it preferentially, as on precision equipment, electronic components, etc. Examples of solvents used are acetone, 1,1,2-trichloro-1,2,2-trifluorethane, 1,1,1-trichloroethane.

solvent dye. See dye, solvent.

solvent extraction. A separation operation that may involve three types of mixture: (1) a mixture composed of two or more solids, such as a metallic ore; (2) a mixture composed of a solid and a liquid; (3) a mixture of two or more liquids. One or more components of such mixture are removed (extracted) by exposing the mixture to the action of a solvent in which the component to be removed is soluble. If the mixture consists of two or more solids, extraction is performed by percolation of an appropriate solvent through it. This procedure is also called leaching, especially if the solvent is water; coffee making is an example. Synthetic fuels can be made from coal by extraction with a coal-derived solvent followed by hydrogenation.
In liquid-liquid extraction one or more components are removed from a liquid mixture by intimate contact with a second liquid that is itself nearly insoluble in the first liquid and dissolves the impurities and not the substance that is to be purified. In other cases the second liquid may dissolve, i.e., extract from the first liquid, the component that is to be purified, and leave associated impurities in the first liquid. Liquid-liquid extraction may be carried out by simply mixing the two liquids with agitation and then allowing them to separate by standing. It is often economical to use counter-current extraction, in which the two immiscible liquids are caused to flow past or through one another in opposite directions. Thus fine droplets of heavier liquid can be caused to pass downward through the lighter liquid in a vertical tube or tower.
The solvents used vary with the nature of the products involved. Widely used are water, hexane, acetone, isopropyl alcohol, furfural, xylene, liquid sulfur dioxide, and tributyl phosphate. Solvent extraction is an important method of both producing and purifying such products as lubricating and vegetable oils, pharmaceuticals, and nonferrous metals.

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